



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 10/656,838 | 09/05/2003 | Jianjun Cheng | ITI-P01-008 | 8403 |

28120 7590 10/18/2006

FISH & NEAVE IP GROUP
ROPES & GRAY LLP
ONE INTERNATIONAL PLACE
BOSTON, MA 02110-2624

| |
|----------|
| EXAMINER |
|----------|

MAIER, LEIGH C

| | |
|----------|--------------|
| ART UNIT | PAPER NUMBER |
|----------|--------------|

1623

DATE MAILED: 10/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

78

| | | | |
|------------------------------|------------------------|---------------------|--|
| Office Action Summary | Application No. | Applicant(s) | |
| | 10/656,838 | CHENG ET AL. | |
| | Examiner | Art Unit | |
| | Leigh C. Maier | 1623 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 July 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-19, 21-26 and 28-39 is/are pending in the application.
- 4a) Of the above claim(s) 21-26 and 28-33 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 34 is/are allowed.
- 6) ☒ Claim(s) 1-19 and 35-39 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>7/20/06</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the Claims

Claims 20 and 27 have been canceled. Claims 1, 3, 4-6, 8, 10, 12, 34 and 35 have been amended. Claims 36-39 are newly added. Claims 1-19, 21-26 and 28-39 are pending. Claims 21-26 and 28-33 are withdrawn as being drawn to non-elected subject matter.

Any rejection or objection not expressly repeated has been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The examiner regrets the oversight in excluding Gonzalez and Kosak in the previous form PTO-892. These references are initialed on the form PTO-1449 which was submitted by Applicant and is appended hereto.

Claim Rejections - 35 USC § 112

Claims 1-19 and 35-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Note that all references to the specification are citing the pre-grant publication US 2004/0077595 for this application.

The claims are now limited to "linear polymers." At paragraph [0082] the disclosure categorizes polymers as "linear, branched or grafted." The difference between "grafted" and "branched" appears to have more to do with how they are made rather than the physical result and would appear to be essentially synonymous with respect to the actual physical structure of the polymer. In this description, the apparent difference between "grafted/branched" and "linear"

Art Unit: 1623

is some sort of linker connecting the backbone and cyclodextrin moiety. However the polymers of the instant claims expressly allow for a polymeric backbone having cyclodextrins attached via linker(s). Therefore, it is not clear what is meant to be excluded when the polymers are recited as being “linear” when the structural formulas appear to allow for a structure that is consistent with the specification’s description of “branched.” The claims are therefore rendered vague and indefinite as one of ordinary skill would not be apprised of the metes and bounds thereof.

Further regarding claim 1, the last two lines of the claim has been amended “wherein either P comprises cyclodextrin moieties alternating with linker moieties in the polymer chain or n is at least 1, wherein at least one linker moiety includes a therapeutic agent.” From reading Applicant’s remarks submitted July 20, 2006, it appears that the intended antecedent for the “linker” in the last line is one of the “alternating linkers” in the penultimate line, so that the required therapeutic agent is covalently attached to one of the “alternating linkers.” However, this particular reading of the claim is not clear from the current wording because there are several “linkers” in the claim. It is the opinion of the examiner that another reasonable interpretation of the claim is that the compound requires at least one linker—somewhere—comprising a therapeutic agent. If the examiner’s interpretation of Applicant’s intent here is correct, it is suggested that the claim be amended to make this clear.

Art Unit: 1623

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 5-19 and 35-38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that Applicant, at the time the application was filed, had possession of the claimed invention.

Claim 1 has been amended as set forth above. Applicant cites the specification at page 16, lines 1-4, for support of this amendment. The passage states “a comonomer A [linker] precursor contains one or more pendant groups with at least one functional group through which reaction and thus linkage of therapeutic agent or targeting ligand can be achieved ...” This supports the concept of an alternating CD-linker structure of the backbone of the polymer. However, it does not support the limitation “wherein at least one linker moiety includes a therapeutic agent.”

It is noted that claim 34 is not included in this rejection because it is the opinion of the examiner that the combination of paragraphs [0080] (comprising the passage of page 16, discussed above) and [0185] support this claim as amended. Paragraph [0080] describes the CD-linker structure, as discussed above. Paragraph [0185] describes a narrower embodiment requiring linearity, water-solubility and a *plurality* of bioactive moieties.

Claim Rejections - 35 USC § 102

Claims 1-3, 5, 7, 10-18 and 35 are rejected under 35 U.S.C. 102(b) as being anticipated by Gonzalez et al (WO 00/01734). Newly added claims 38 and 39 are also included in this rejection.

As Applicant notes, new claim 39 corresponds to original claim 1, incorporating subject matter from claims 12 and 35. As such, this claim is subject to the same rejection used previously for claims 1, 12 and 35.

Gonzalez teaches as set forth in the previous Office action. Applicant contends that the reference “does not teach or suggest a polymeric compounds comprising cyclodextrin moieties alternating with linker moieties in the polymer chain ... wherein at least one linker moiety includes a therapeutic agent.” As discussed above, it appears that Applicant intends that the intended antecedent for the “linker” in the last line of the amended claim is one of the “alternating linkers” in the penultimate line of said claim, so that the required therapeutic agent is covalently attached to one of the “alternating linkers.” The examiner disagrees because of the multiple “linkers” in the claim to which this might refer. Therefore, the examiner maintains that the exemplified product meets the limitations of the claims. For example, in claim 1, this linker to which the therapeutic agent is attached could be L₂, one that is not required to be attached to one of the “alternating” linkers.

Regarding claim 3, Applicant contends that the reference does not teach or suggest linear polymeric compounds with one or more cyclodextrin groups not part of the polymer chain. The examiner respectfully disagrees with this interpretation of the requirements of the claim. The claim requires that a cyclodextrin and a therapeutic agent be present. However, there is no

Art Unit: 1623

limitation on the identity of “P,” the monomer, which could be a cyclodextrin, and the variable “n” can be zero.

Claims 3-5, 7, 10-16, 19 and 35 are again rejected under 35 U.S.C. 102(b) as being anticipated by either of (1) Hristova-Kazmierski et al (Bioorg. Med. Chem. Lett., 1993)—also claim 6; (2) Minami et al (J. Pharm. Sci., 1998)—also claims 8 and 9; (3) Yano et al (J. Pharm. Sci., 2001)—also claims 8 and 9; or (4) Tanaka et al (US 5,183,883)—also claims 8 and 9, as set forth in the previous Office action. Newly added claims 36-38 are also included in this rejection.

Applicant’s arguments filed July 20, 2006 have been fully considered but they are not persuasive. Applicant submits that claims 3 and 4 have been amended so that the compounds are now linear polymeric ones. The examiner agrees that the compounds are now recited as being linear polymeric ones. However, the value for the variables “o” in claim 3 and “h” in claim 4 has the range of “1 to 30,000.” Therefore, although the compounds are described as polymeric, the stated structural requirements allow for a monomeric compound, so the descriptor “polymeric” is not given patentable weight, and the claims are construed with the minimum requirements discussed in the previous Office action.

Claim Rejections - 35 USC § 103

Claims 1-3, 5, 7, 12-19 and 35 are again rejected under 35 U.S.C. 103(a) as being unpatentable over Gonzalez et al (WO 00/01734). Newly added claims 36-39 are included in this rejection.

Gonzalez teaches as set forth in the previous Office action. As noted above, Applicant contends that the reference “does not teach or suggest a polymeric compounds comprising cyclodextrin moieties alternating with linker moieties in the polymer chain ... wherein at least one linker moiety includes a therapeutic agent.” The examiner agrees that the exemplified product does not appear to meet this limitation. However, the reference does, in fact, suggest such a product. See paragraph bridging pages 13 and 14. “[T]he additional ligand or ligands may be bound to the same or different cyclodextrin moiety or *the same or different comonomer A* of the copolymer.” (emphasis added) Furthermore, the reference expressly suggests the use of comonomers having functional groups suitable for attaching said ligands. See page 11, lines 19-30. The examiner reiterates that the agents termed “ligands” in the reference would also include entities that would be considered therapeutic agents. With respect to new claims 36 and 37, the reference suggests the use of high molecular weight products, such as proteins and polysaccharides, which would be expected to result in a product consistent with these claims.

Double Patenting

Claims 1-3, 5, 7, 12-19 and 35, as amended, are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over (1) claim 7 of U.S. Patent No. 6,884,789 or (2) claim 4 of U.S. Patent No. 6,509,323. Although the conflicting claims are not identical, they are not patentably distinct from each other. The instant claims are drawn to CD-polymers requiring the covalent attachment of a therapeutic agent. The CD-polymers recited in the cited patents require the covalent attachment of a targeting ligand. As discussed above, these categories are overlapping. Reference claims 3 and 8, respectively, recite the use of linkers

Art Unit: 1623

comprising functional groups suitable for attaching a ligand, as suggested in the written description of the products. See col 9, lines 10-29 of '323 and col 10, lines 38-60 or '789.

Allowable Subject Matter

Claim 34 is allowed.

The following is a statement of reasons for the indication of allowable subject matter:

Gonzalez teaches as set forth above. As discussed, the reference does suggest the attachment of ligands to linkers in CD-linker copolymers and “ligands” (reference) and “therapeutic agents” (invention) are overlapping categories. However, the intended use of the reference compounds is in a manner whereby the linked entity acts as a ligand or targeting agent. Therefore, the examiner finds no teaching or particular motivation to prepare a product wherein the ligand is attached to one of the “alternating linkers” and is attached via a biohydrolyzable bond. The exemplified product (ligand not attached to alternating linker) happens to comprise a hydrolysable amide bond, but the reference provides no particular direction regarding these attachments in general.

Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period

Art Unit: 1623

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

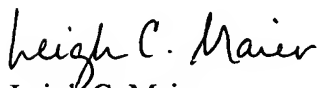
however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Examiner's hours, phone & fax numbers

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh Maier whose telephone number is (571) 272-0656. The examiner can normally be reached on Tuesday, Thursday, and Friday 7:00 to 3:30 (ET).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Anna Jiang (571) 272-0627, may be contacted. The fax number for Group 1600, Art Unit 1623 is (571) 273-8300.

Visit the U.S. PTO's site on the World Wide Web at <http://www.uspto.gov>. This site contains lots of valuable information including the latest PTO fees, downloadable forms, basic search capabilities and much more. Information regarding the status of an application may be obtained from the Patent Application Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished application is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov> Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.



Leigh C. Maier
Primary Examiner
October 13, 2006